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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 415WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/DK 03/00907	International filing date *(day/month/year)* 18.12.2003	Priority date *(day/month/year)* 23.12.2002
International Patent Classification (IPC) or both national classification and IPC C07C253/34		
Applicant H.LUNDBECK A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07.06.2004	21.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Breimaier, W Telephone No. +49 89 2399-8327

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK 03/00907

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-28 as originally filed

Claims, Numbers

1-29 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-27, 29
	No:	Claims	28
Inventive step (IS)	Yes:	Claims	1-27, 29
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-29
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:
D1: EP-A 0 347 066

The present invention concerns a method for making racemic citalopram diol, R- or S-citalopram diol which in a subsequent ring closing reaction furnish the corresponding citalopram according to claims 1 to 29.

novelty

a. The present application does not meet the criteria of Art. 33(1) PCT, because the subject-matter of claim 28 is not new in the sense of Art. 33(2) PCT.

The use of R,S-diol, R- and S-diol for making the corresponding citalopram is already known in the art (see e.g. D1, reaction schemes I and II).
In that connection it is noted that a compound is not rendered novel by its new preparation method.

b. The present subject-matter according to claims 1 to 27 and 29 is novel (Art. 33(2) PCT).
In the closest state of the art D1 the diol II or the enantiomerically pure diol II is esterified which in the presence of a base undergoes stereoselective ring closure to the corresponding enantiomerically pure citalopram (see reaction schemes I and II). In the present method the racemic diol and S- or R-diol is obtained by separation of the initial non-racemic R,S-diol into a racemic R,S-diol as a precipitate and the isolation of R- or S-diol from the mother liquor as claimed in claim 1. The so-obtained racemic diol and R- or S-diol furnish the corresponding citalopram by ring closure.

inventive step

The present subject-matter is considered to be inventive in the sense of Art. 33(3) PCT.

In view of D1 the problem posed is the provision of an alternative method for making racemic citalopram and/or S- or R-citalopram. This is solved by the present separation method of a non-racemic mixture of R,S-diol into a racemic R,S-diol precipitate and the isolation of R- or S-diol from the mother liquor. This finding has been shown in the examples. In the available prior art there is no indication which would have led the

skilled person to the present solution in order to get the required enantiomerically pure racemic diol and R- or S-diol to be used for making citalopram.
Thus, an inventive step can be acknowledged.

further remarks
for clarity (Art. 6 PCT) the following needs to be taken care of:
a. Although the expressions "racemic diol, S-, R-, R,S-diol" do have a specific meaning in the present case, these expressions are not defined in independent claim 1.
b. Furthermore, in Claim 1, i) and iii), the matter for which protection is sought is not clearly defined. In the present case the **acid** and the **solvent** used are essential technical features in order to successfully carry out the present invention. However, these features are not specified in accordance with the present disclosure.
c. Claims 8 and 27 define the result to be achieved rather than a further technical process feature.
d. The description is not adapted to the amended set of claims.